indomethacin, piroxicam, ketoprofen, etodolac, diflusinal, meloxicam, aceclofenac, fenoprofen, naproxen, tiaprofenic acid, and tolmetin.

Please cancel claim 8, without prejudice.

REMARKS

Claims 1-7 and 9-11 are pending in the application. Claims 1, 2, and 9 have been amended. No new matter is added by the amendments. Support for the amendments to the claims is found at least in the specification at page 5, lines 4-8 and in claims 8 and 9 as originally filed. A marked-up copy of the amended claims 1, 2 and 9 is enclosed pursuant to 37 C.F.R. § 1.121.

New claims 15-17 are added, but contain no new matter. Support for the new claims is found at least in claim 9 as originally filed, and in the specification, at least at page 6, line 29 to page 7, line 4.

In Paper No. 8, the Examiner has maintained the rejection of claims 1-11 under 35 U.S.C. § 103(a) asserting that the claims are unpatentable over U.S. Patent No. 6,096,728 of Collins, *et al.* ("Collins") taken in view of U.S. Patent No. 5,811,425 of Woods, *et al.* ("Woods"). Specifically, the Examiner contends that Collins teaches an emulsion that comprises COX-2 inhibitors and Woods teaches an emulsion comprising castor oil (a hydroxylated vegetable oil) and a COX-2 inhibitor. The applicants respectfully traverse this rejection.

Collins teaches a pharmaceutical composition for treatment of interleukin-1 (IL-1) mediated inflammatory diseases. The Collins composition contains a controlled release polymer and a proteinaceous IL-1 inhibitor. Polymers for use in the Collins composition include bulk erosion polymers, surface erosion polymers, cellulose, hyaluronan, alginate, collagen, gelatin, albumin, starches and dextrans. The Collins composition may include a non-steroidal anti-inflammatory drug and/or an analgesic. The Collins composition does not contain a drug for use in the treatment of impotence. Further, as the Examiner has conceded in Paper No. 6, Collins does not teach inclusion of a hydroxylated oil in the composition.

At column 26, lines 33-36, Collins teaches that, once the Collins composition has been formulated, it "may be stored in a sterile vial as a solution, suspension, gel, emulsion, solid, or dehydrated or lyophilized powder." No specific type of emulsion is described or disclosed.

Even assuming Collins teaches an emulsion, Collins does not teach which phase of "an emulsion" the IL-1 inhibitor of Collins or any other of the active agents disclosed in Collins may be suspended, nor does it teach that an oil phase of the Collins emulsion contains more than 50% of the active agent dissolved therein.

Woods teaches a COX-2 inhibitor of a specific structure. This COX-2 inhibitor can be incorporated into a pharmaceutical composition for sterile parenteral injection, including pharmaceutically acceptable sterile aqueous or non-aqueous solutions, dispersions, suspensions or emulsions, as well as sterile powders. Examples of suitable aqueous and non-aqueous carriers, diluents, solvents, or vehicles, as disclosed in Woods, include water, ethanol, polyols, vegetable oils (such as olive oil), and injectable organic esters. Liquid dosage forms for oral administration taught in Woods include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs.

Woods teaches that, in addition to the active compounds, the liquid dosage forms may contain diluents. A long list of the suggested diluents is provided: water, ethyl alcohol, isopropyl alcohol, ethyl carbonate, ethyl acetate, benzyl alcohol, benzyl benzoate, propylene glycol, 1-3 butylene glycol, dimethyl formamide, and oils (in particular, cottonseed, groundnut, corn, germ, olive, castor, and sesame). Woods does not make a specific disclosure of any particular type of emulsion, and certainly does not specify that the COX-2 inhibitor of Woods can be suspended in an oil-in-water emulsion, nor does it articulate that the COX-2 inhibitor is dissolved in the oil phase of the oil and water emulsion in any amount. Further, there is no specific disclosure in Woods of an oil-in-water emulsion that utilizes a hydroxylated oil.

To establish *prima facie* obviousness, the Examiner must demonstrate (i) that the suggested combination teaches or suggests each element of the claimed invention; (ii) that there is some motivation in the art for a person of ordinary skill to make the combination proposed by the Examiner; and (iii) that a person of ordinary skill would have had a reasonable expectation that such modification would be successful.

First, the Collins-Wood combination does not teach or suggest each element of the claimed invention. As the applicants have explained previously, neither Collins nor Woods teaches an oil-in-water emulsion in which a non-steroidal anti-inflammatory drug is suspended. Rather, Collins generally teaches that the finished Collins composition can be stored in a sterile vial as "an emulsion." Similarly, Woods does not teach a specific type of emulsion, and certainly

does not specify that the COX-2 inhibitor of Woods is to be suspended in an oil-in-water emulsion containing hydroxylated oil. Woods teaches that hydroxylated oil (caster oil) is to be used as a diluent, not in the preparation of any type of emulsion.

A person of ordinary skill in the art would have recognized that the term "emulsion" is a generic term that encompasses more than one type of emulsion. For example, Chambers Dictionary of Science and Technology specifies that an "emulsion," in the chemical arts, is a "colloidal suspension of one liquid in another." It is not required or specified that an emulsion is a suspension of an oil in water, as the Examiner seems to be stating. *See, Walker, ed.,* Chambers Dictionary of Science and Technology, Chambers Harrap Publishers, Ltd., New York, 1999, p. 395, attached hereto. Further, a person of ordinary skill in the art would have understood that a mere general disclosure of an emulsion, as provided in both Collins and Woods, is not the same as the specific disclosure of a specific type of emulsion.

In support of this position, the applicants provide herewith the Declaration of Lisbeth Illum, an inventor of this application and a person whose background and experience make her at least one of ordinary skill in the art. Declaration of Lisbeth Illum, ¶¶ 1 and 2. The disclosure of a generic emulsion would not have provided the skilled person with any teaching as to the specific type of emulsion that is used in the compositions of the invention as claimed. Declaration of Illum at ¶ 7. An emulsion is a colloidal suspension of one liquid in another. *Id.* at 8. A person of ordinary skill in the art is knowledgeable as to the different types of emulsions, and oil-in-water emulsions are simply one of these. *Id.; see, e.g., Remington: The Science and Practice of Pharmacy,* page 323, Decl. of Illum at Exh. A. For example, emulsions may exist as multi-phase emulsions, or double-phase emulsions. *Id.*

Neither Collins nor Woods teaches or suggests the specific type of emulsion preparation into which the Collins or Woods compositions may be incorporated. Further, neither Woods nor Collins teaches or suggests an emulsion into which more than 50% (weight basis) of the drug is dissolved in the oil phase of an oil-in-water emulsion.

Additionally, even if the Collins-Woods combination did teach or suggest each element of the invention as claimed, a person of ordinary skill would not have been motivated or provoked to make the combination (and the necessary modification) in order to arrive at the present invention. Neither Collins nor Woods discloses use of emulsions, let alone oil-in-water emulsions suitable for compositions for nasal administration. Collins discloses preparations that

may contain anti-inflammatory compounds for oil or injectable administration. Col. 34, line 30 to col. 35, line 30. Similarly, Woods describes oral formulations. Accordingly, a person seeking to make and oil-in-water emulsion pharmaceutical composition suitable for nasal administration in which more than 50% of the drug was suspended in the oil phase of the oil-in-water emulsion would not seek out the teachings of either Collins or Woods and combine them (with the modification) in order to arrive at the present invention, nor would he reasonably expect that such combination would give rise to a successful result, as it is well known in the art that suitable vehicles for oral administration are not necessarily effective or useful if applied to compositions for nasal administration.

Accordingly, for the reasons set forth above, it is respectfully requested that the Examiner reconsider and withdraw the 35 U.S.C. § 103 rejection based upon Woods and Collins.

Respectfully submitted,

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(Date)

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Enclosures

Marked-Up Version of Amended Claims 1, 2, and 9

1. (Twice amended) A pharmaceutical composition adapted for nasal administration comprising

(i) an oil-in-water emulsion and

(ii) a drug *that is* dissolved in the emulsion, *wherein more than 50% of the drug on a weight basis is dissolved in the oil phase of the emulsion,*

wherein the oil phase comprises a hydroxylated oil, and the drug is for systemic delivery and is selected from the group consisting of an analgesic agent, a drug for the treatment of Parkinson's disease, a drug for the treatment of impotence, and a non-steroidal anti-inflammatory drug, but wherein the drug is not a cannabinoid.

2. (Twice amended) A composition adapted for nasal administration comprising

(i) a oil-in-water emulsion and

(ii) a drug *that is* dissolved in the emulsion, *wherein more than 50% of the drug on a weight basis is dissolved in the oil phase of the emulsion,*

wherein the oil phase comprises a hydroxylated oil, and the drug is for systemic delivery and is selected from the group consisting of an analgesic agent, a drug for the treatment of Parkinson's disease, a drug for the treatment of impotence and a non-steroidal anti-inflammatory drug, but wherein the drug is not a cannabinoid, for use in medicine.

9. (Amended) A composition according to *claim 1*, wherein more than 75 % of the drug is dissolved in the oil phase on a weight basis.